SYNOPSIS

Dendrimers are hyperbranched macromolecules, with branches-upon-branches architectures, precise constitutions and molecular weights of several kilo Daltons These macromolecules are characterized by their monodispersities and nanometric dimensions Research in the area of dendrimer chemistry has evolved during last nearly one and half decades The initial efforts in the development was concerned largely with identification of synthetic methodologies for the synthesis of dendrimers Exploring these macromolecules in a variety of chemical, biological and materials studies have been undertaken in the last few years Evidently the dendritic architecture remains to be the most influential in larger developments of dendrimer chemistry at present

Incorporation of catalytically active metal ions in dendrimers is being considered in detail, as the dendritic architecture offer advantages not only of the traditional homogeneous and heterogeneous catalysis, but also in the evolution of the so-called dendritic effect, which modulate the functional properties of such dendrimers. The evolution by the dendritic effect is unique for dendrimers and such architecturally driven effects are not easily achievable with other molecular and macromolecular architectures Incorporation of the metal ions both inside and peripheries of dendrimers has been identified and a number of studies have been conducted The **Chapter 1** of the Thesis provides a broad overview of the dendrimer chemistry and the studies of dendrimer for organometallic catalysis

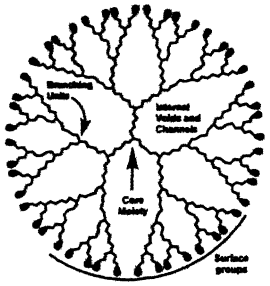

Figure 1. Cartoon representation of dendrimer

A number of monomers have been identified for the construction of dendrimers, either by a divergent growth or convergent growth methodologies In spite of the identification of a number of monomers and dendrimers there upon, only few dendrimers namely,

poly(amido amine), poly(propylene imine), poly(benzyl aryl ether), phosphorous and silane based dendrimers, occupy most of the studies that have been carried out so far in dendrimer chemistry Identification of new monomers and synthesis of new dendrimers is a continuously evolving interest In this respect, synthesis of new poly(alkyl ether imine) dendrimers were undertaken in this Thesis The use of 3-amino-propan-1-ol as a new monomer was been exploited in order to synthesize poly(propyl ether imine) dendrimers An iterative synthetic sequence of two alternate Michael additions and two alternate reduction reactions were identified to construct poly(propyl ether imine) dendrons and dendrimers, in which the cores were either a benzenoid or an oxygen or a nitrogen were synthesized, either by a convergent or a divergent synthetic methodology The structures of an oxygen core and a nitrogen core dendrimers are presented in **Figure 2** The divergent methodology has been established to be more facile and each individual steps of dendrimer synthesis was found to be excellent

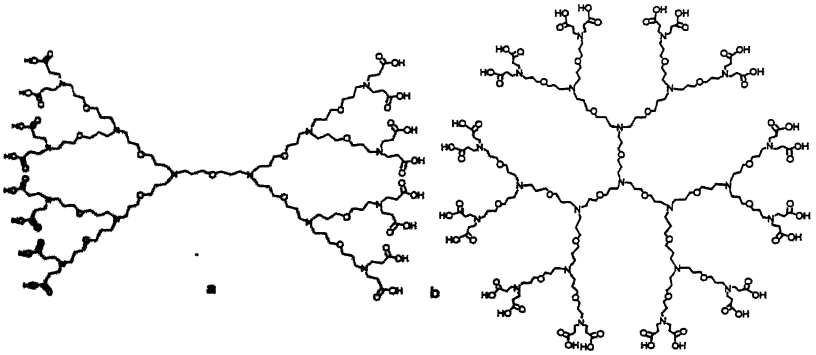

Figure 2. Molecular structures of third generation oxygen (a) and nitrogen core (b) dendrimers, with carboxylic functionality at the periphery.

Upon synthesis of water-soluble carboxylic acid terminated dendrons and dendrimers, their biological properties were established, primarily due to the constitution of poly(ether imine) dendrimers, resembling closely to that of biologically relevant poly ethers and poly

amines The cytotoxicity tests, performed with the aid of MTT assay, revealed that the poly(ether imine) dendrons and dendrimers were non-toxic, in that the live cells survivability were found to be more than 95 % **Chapter 2** of the Thesis elaborates design, synthesis, characterization and biological evaluation of several poly(ether imine) dendrons and dendrimes

The poly(propyl ether imine) dendrimers can be presented with either an alcohol, or amine or a carboxylic acid or a nitrile at their peripheries This broad choice of functional groups possible at the peripheries of dendrimers opened up opportunities to conduct metal complexation studies with these dendrimers In the first part of the research, organometallic catalysis with the dendrimers was undertaken, in order to evaluate the catalytic efficacies of dendrimer based organometallic catalysis Thus, the peripheries of hydroxy terminated poly(propyl ether imine) dendrimers were further functionalized with a chloride, followed by the conversion of chloride to alkyl diphenyl phosphine In this manner, 2, 4, 8 and 16 alkyl diphenyl phosphines were installed at the peripheries of the poly(propyl ether imine) dendrimers Upon synthesis, their metal complexation with Pd^{II} was performed, so as to realize metallation of bidentate alkyl diphenyl phosphine-Pd^{II} moieties at the peripheries of dendrimers Zero, first, second and third generation dendrimers were thus possessing 1, 2, 4 and 8 such catalytic units at these peripheries, respectively. **Figure 3** shows the third generation alkyl diphenyl phosphine-Pd^{II} complex. The catalytic efficacies of these dendrimers were tested in the prototypical organic transformation, namely, the Heck coupling of C-C

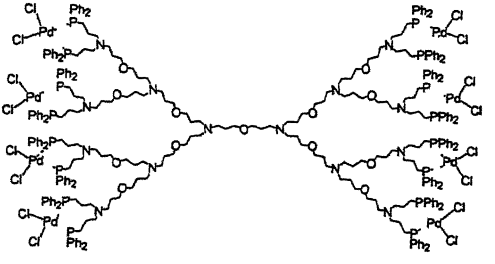

Figure 3. Structure of third generation PETIM dendrimer modified with $Pd(PPh_2)Cl_2$ complexes.

bond formation These studies revealed that while the conversion of the reaction of various alkenes with iodobenzene in the presence of dendritic catalysts were lowered as the generation number advanced, the ratio of the catalyst required and the corresponding turn-over-numbers were higher for the higher generation dendritic catalyst, when compared to the lower generation catalyst **Figure 4** shows the turn-over-number *vs* the olefinic substrates with which the Heck coupling was performed **Chapter 3A** of the Thesis describes synthesis, characterization and catalysis studies of poly(propyl ether imine) modified with alkyl diphenyl phosphine-Pd^{II} moieties

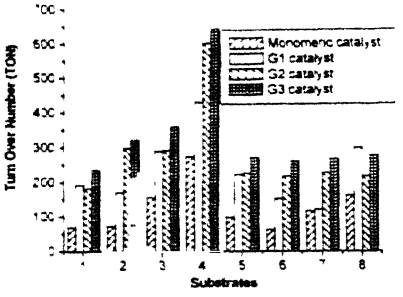

Figure 4 A plot of turn-over-number calculated for the Heck coupling reaction of iodobenzene with various olefinic substrates (1 = styrene, 2 = methylacrylate, 3 = ethylacrylate; 4 = *t*-butylacrylate, 5 = acrylonitrile, 6 = 2-cyclohexenone, 7 = 2-cyclopentenone and 8 = 2-acetamidomethyl acrylate)

The newly synthesized poly(propyl ether imine) with carboxylic acid at the peripheries possess amine and carboxylic acid donor sites for metal complexation. Ligands such as diethylenetriaminepentacetic acid (DTPA) are excellent examples for metal coordination For instance, DTPA-Gd^{III} metal complex, chelating through the available amine and carboxylic acid sites, has a dissociation constant exceeding 10^{-25} M. With the features of poly(ether imine) dendrimers, possessing with amine and carboxylic acid chelation sites, the metal ion uptake properties of these dendrimers with a lanthanide metal ion, namely, Gd^{III} was undertaken. The extent of metal ion complexation was assessed with the aid of Uv-Vis spectroscopic method involving an established chromogen, namely, arsenazo III. This study allowed [illegible] of the number of Gd^{III} complexed with each ligand. Table 1 presents the results of this study.

In order to assess the associated stability constants of the multivalent dendritic ligar and its Gd^{III} metal complex, preliminary potentiometric studies were initiated Tr protonation behaviour of the multivalent ligand and its metal complex was assessed in th range of pH 2 5-10 It was observed that while the ligands alone generally showed monophasic protonation behaviour, that o the metal complexes were observed to be more complex and a straightforwarc correlation of the protonation behaviour was not obvious **Chapter 3B** of the Thesis describes the Gd^{III} metal complexation studies with dendritic ligands and the results of the potentiometric studies

	Ligand Structure	Ratio of Gd^{III} to ligand
1	*p*-MethoxyDendron G2	1 ± 0 15
2	*p*-MethoxyDendron G3	1 8 ± 0 18
3	O-Core Dendrimer G1	1 ± 0 09
4	O-Core Dendrimer G2	1 7 ± 0 36
5	O-Core Dendrimer G3	3 6 ± 0 54
6	Benzene Dendrimer G1	1 ± 0 27
7	Benzene Dendrimer G2	2 5 ± 0 33

Table 1 Ratio of Gd^{III} to dendrimer ligand, determined by Uv-Vis spectrophotometry

Metal ion complexation properties of dendrimers was studied further, in this instance the metal ion complexation was performed, so as to install the metal ion as the core of dendrimers T he m etal ion c omplexation w as e nvisaged further t o i nvolve t he a mine a nd carboxylic acid donor sites In these efforts, the well-established poly(benzyl aryl ether) dendrimers were used to study the metal complexation properties. Thus, poly(benzyl aryl ether) dendrimers functionalized with an amino acid, namely

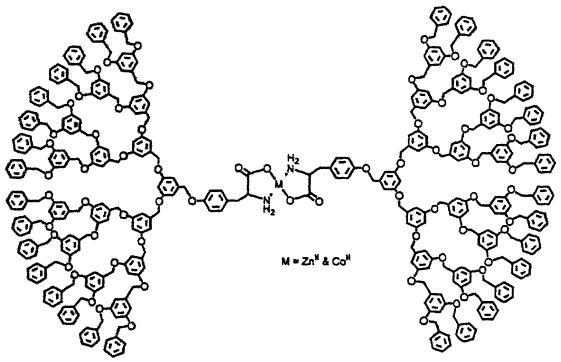

Figure 5 Structure of fourth generation poly(aryl ether) dendrimer-metal complex

tyrosine, were synthesized up to four generations The phenolic hydroxyl group of tyrosine was linked to the poly(benzyl aryl ether) dendrons, whereas the α-amino acid portion was utilized for the metal ion coordination The transition metal ions, namely Co^{II} and Zn^{II}, were undertaken for studies of the dendron encapsulation **Figure 5** shows the fourth generation dendron-Zn^{II} metal complex Upon synthesis of a series of zero to fourth generation of dendrimers, constituted with a metal ion core, optical rotation properties were studied first These studies revealed that while the molar rotation remained nearly constant across the series of dendrimers, the specific rotation itself, arising form the tyrosine unit was found to be decreasing as the generation advanced and this effect appeared to arise from the so-called 'optical dilution', wherein the number of chiral centers remained the same, even while the molecular weights of the series of dendrimers increased exponentially The corresponding Co^{II}-cored dendrimers were accessible to Uv-Vis spectroscopic studies The coordination geometry and the stoichiometry of metal ion to dendron was established firmly with the Co^{II}-cored dendrimers These dendrimers were further investigated for their electroactive properties Thus, cyclic voltametric studies were conducted in order to assess the Co^{II} - Co^{I} - Co^{0} redox properties These studies revealed an ensuing dendritic effect, in that the reduction potential of $Co^{II} \rightarrow Co^{I}$ was decreasing as the generation number increased form zero to one to two The redox behavior arising from the third and fourth generation dendrimer were not facile and it seemed that these larger generation dendrimers deposited on the electrodes and the redox reaction of cored Co^{II} metal ion became more difficult

Chapter 4 of the Thesis describes synthesis, characterization, optical rotation, Uv-Vis spectroscopic and cyclovoltametric studies of metal ion (Zn^{II}, Co^{II}) cored poly(benzyl aryl ether) dendrimers

Overall, the studies in this thesis will cover establishing a synthetic methodology for the synthesis of a series of poly(ether imine) dendrimers, their conversion to catalytically

active alkyl diphenyl phosphine-Pd^{II} complexes and Gd^{III} complexes To the extent that ethe and imine acting as linker and branching components, respectively, these dendrimers posses. properties analogous to polyethers and polyamines. Research work carried out further or dendronized amino-acid metal complexes and their optical, spectroscopic and electro active properties will be discussed further in the Thesis

Results from few of the above chapters are published in the following publications

(1) Krishna, T R, Jayaraman, N 'Dendritic encapsulation of aminoacid-metal complexes Synthesis and studies of dendron functionalised L-tyrosine metal (Zn^{II}, Co^{II}) complexes' *J Chem Soc, Perkin Trans 1* **2002**, 746 - 754.

(2) Krishna, T. R, Jayaraman, N 'Synthesis of poly(propyl ether imine) dendrimers and evaluation of their cytotoxic properties' *J Org Chem* **2003**, *68*, 9694-9704

(3) Krishna, T R, Jayaraman, N 'Synthesis and catalytic activities of Pd^{II}-phosphine metal complexes modified poly(ether imine) dendrimers' *Tetrahedron* **2004**, *60*,10325-10334

(4) Krishna, T. R, Mukta, B, Tatu, U, S, Jayaraman, N 'Synthesis and *in vivo* studies on water soluble poly(propyl ether imine) dendrimers' submitted

(5) Krishna, T R, Jayaraman, N 'Dendrimers as multitopic ligands for lanthanum salts· An evaluation of the Gd^{3+} uptake properties of PETIM dendrimers' manuscript under preparation